AMENDMENTS TO THE SPECIFICATION

Please amend paragraph [0005], that appears on page 3, to read:

The main focus of researchers and the principal aim of those associated with drug development for AD is to reduce the amount of Aβ ~~A-β~~ deposits in the central nervous system (CNS). These activities fall into several general areas: factors affecting the production of ~~A-β~~ Aβ, the clearance of ~~A-β~~ Aβ, and preventing the formation of insoluble ~~A-β~~ Aβ fibrils. Another therapeutic goal is to reduce inflammatory responses evoked by Aβ neurotoxicity. Several groups have demonstrated the ability of the Alzheimer's disease toxin, ~~A-β~~ Aβ 1-42, to induce antibody titers in either wild-type, APP, or APP/PS1 transgenic mice (Schenk et al. 1999, Janus et al. 2000, Morgan et al. 2000). Sufficient immunization with peptide also leads to reduction in amyloid burden and improved cognition in transgenic mice. Apparently, more than one mechanism contributes to antibody efficacy, including sequestering of ~~A-β~~ Aβ peptides in the periphery and induction of Fc-γ receptor mediated phagocytosis by microglia in the brain. Frangionne et al., (PCT/US01/16322) demonstrated that a shortened version of the ~~A-β~~ Aβ 1-42 toxin can also be used to induce antibodies and reduce amyloid burden in a transgenic model of AD. This peptide includes the first 30 amino acids of ~~A-β~~ Aβ 1-42 plus a N-terminal tail of six lysine residues; it has the added advantage of not being fibrillogenic or cytotoxic in vitro. Additional modifications to the 1-30 amino acid peptide have been proposed, including substitutions at amino acids 17-21 and N- or C-terminal additions, that will confer both reduced fibrillogenicity/toxicity and improved immunogenicity in the vaccinated host.

Please amend paragraph [0033], that begins on page 12, to read:

Their predictive accuracies are considerable. On the other hand, neural networks are more complex, nonlinear and self learning systems. Their predictive accuracies are higher but they require large amount of data for learning which makes Quantitative matrix based methods suitable for MHC binding peptide predictions. Structure based methods are logically very sound but

computationally complex. These methods calculate binding energy of peptide-MHC complex and the energetically favorable peptides are predicted as binders. These methods are in stages of development. All the above mentioned approaches cannot effectively deal with MHC ~~Polymorphism~~ polymorphism i.e. for each allele a separate matrix has to be generated or a separate set of rules have to be applied. Recently, Stumiolo et al., 1999 provided an answer by using virtual matrix which holds promise for delivering better MHC binding peptide prediction method. Publicly accessible algorithms from the BioInformatics & Molecular Analysis Section (BIMAS) of the National Institutes of Health rank potential peptides based on predicted half-time of dissociation to HLA class I molecules. They are based on coefficient tables deduced from the published literature by Dr. Kenneth Parker (Parker 1994), Applied Biosystems (see website ~~http://bimas.dcrt.nih.gov/molbio/hla_bind/~~ bimas.dcrt.nih.gov/molbio/hla_bind/). Additional programs and databases that could be used for prediction of epitopes for both class I and/or class II molecules are found, for example, at the SYFPEITHI website (~~http://syfpeithi.bmi-heidelberg.com/sc--ripts/MHCServer.dll/home.htm~~ syfpeithi.bmi-heidelberg.com/sc-ripts/MHCServer.dll/home.htm) and the HIV Molecular Immunolgoy Database website (~~http://hiv.basic.nwu.edu/HLA/MotifScanner.cfm~~ hiv.basic.nwu.edu/HLA/MotifScanner.cfm) and the Molecular Immunology Foundation Tools for Science website--RANKPEP (~~http://mif.dfci.harvard.edu/Tools/~~ mif.dfci.harvard.edu/Tools/). The step of determining the resulting score of all amino acid of the subsequence based on each of the binding value of each amino acids obtained in step a is conducted by addition of each of the amino acid values and by simply adding the values or multiplication. In another embodiment, the determining step so as to obtain a resulting score can be performed by using a complex mathematical function. The resulting score is compared to preselected value or preselected score, to predict presence of undesirable T-cell epitopes within amyloid beta peptide or homologue thereof.

Please amend paragraph [0068], that appears on page 30, to read:

According to the allele frequencies of serologically typed HLA loci reported at the XIth Workshop (~~http://histo.chu-stlouis.fr/inserm/marc/St--ats/statser.htm~~ histo.chu-stlouis.fr/inserm/marc/St- ats/statser.htm), the four most common HLA-A molecules in the U.S.

Caucasian population are A1 (16.9%), A2 (28.3%), A3 (12.2%), and A24 (9.6%). Additional statistics on the frequency of HLA-A, B, and C molecules can be found in the book entitled The HLA Factsbook (Academic Press, 2000). Screening of peptide Abeta K6-1-30-LV/EE for these prevalent alleles gives the results shown in Table 5. No epitopes of significance are predicted to bind to HLA-A2_01, A2_05, or A3 molecules (Table 5c-d). The very low score of the highest ranked epitope for the HLA-A24 molecule (score of 2.2; Table 5e) suggests that this will also not be if significance. The HLA-A1 allele, on the other hand, shows binding to an epitope from the Abeta K6-1-30-LV/EE with a score of 18 (Table 5a). If this epitope is validated in in vitro assays (see below), it would be prohibitive to administer the K6-1-30-LV/EE peptide to individuals displaying the HLA-A1 molecule. It is important to note that the addition of the K6 motif at the N-terminus of ~~Ab~~ Aβ1-30 does not introduce any epitopes of significance for the above-mentioned HLA alleles.

Please amend paragraph [0069], that appears on page 33, to read:

According to the allele frequencies of serologically typed HLA loci reported at the XIth Workshop (~~http://histo.chu-stlouis.fr/inserm/marc/St- ats/statser.htm~~ histo.chu-stlouis.fr/inserm/marc/St- ats/statser.htm), the most common HLA-B molecules in the Japanese (Wajin) population are B52, B61, B51, B62, and B35. Screening of peptide ~~Abeta~~ Aβ K6-1-30-LV/EE for these prevalent alleles gives the results shown in Table 5. No epitopes of significance are predicted to bind to HLA-10 B_5201, B_5101, B_5102, B_5103, B62, or B_3501 molecules (Table 6a, c-g). The BLA-B61 allele, on the other hand, shows binding to an epitope from the Abeta K6-1-30-LV/EE with a score of 40 (Table 6b). If this epitope is validated in in vitro assays (see below), it would be prohibitive to administer the K6-1-30-LV/EE peptide to individuals displaying the HLA-B61 molecule. It is important to note that the addition of the K6 motif at the N-terminus of ~~Ab~~ Aβ1-30 does not introduce any epitopes of significance for the above-mentioned HLA alleles.

Please amend the citation found at page 53, lines 12-15 to read:

Rammensee, Hans-Georg, Jutta Bachmann, Niels Nikolaus Emmerich, Oskar Alexander Bachor, Stefan Stevanovic: SYFPEITHI: database for MHC ligands and peptide motifs.

Immunogenetics (1999) 50: 213-219 (access via: ~~http://www.uni-tuebingen.de/uni/kxi/~~ www.uni-tuebingen.de/uni/kxi/)